Real-time detection of the start and subsequent epidemic states of HIV outbreaks among people who inject drugs: insights from four European countries

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Injecting drug use and HIV in Europe

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- No automated real-time outbreak detection system has been developed for monitoring HIV among PWID yet.

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    - Hidden Markov Model (HMM)
    - Bayesian methods
- Although novel methods seem promising, most comparative studies focused on the classic ones and were based on simulations.

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- Unlike other epidemics widely investigated, HIV outbreaks among PWID differ in their:
    - ◇ size
    - ◇ duration and
    - ◇ post-epidemic level.
- Research questions on how anomaly detection methods behave when applied to such epidemic curves remain still open.

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of HIV outbreaks among PWID in four European countries.

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- a novel approach HMM-PI that combines the former two
- control charts for outbreak detection
  - ◇ Exponentially Weighted Moving Average (EWMA) and
  - ◇ Cumulative Sum (CUSUM) chart for Poisson variate.

Methods: Overview (2)

Detection of epidemic states was sequentially conducted

Pre-epidemic state → **Growth** → **Decline** → **Post-epidemic state**

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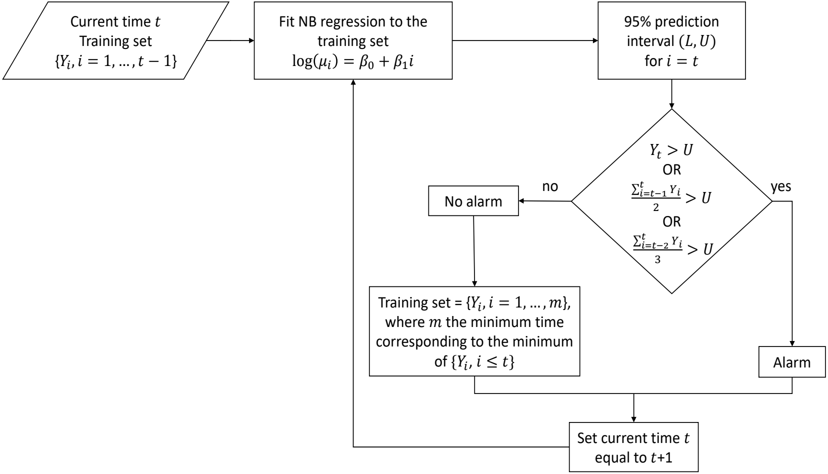
Baseline (i.e., counts without outbreaks): historical pre-epidemic cases extending three years in total

Constraint: ≥ 12 observations in training set i.e., once the epidemic state changed, it remained unchanged for the following 11 weeks

Growth phase: Method based on prediction interval (PI)

Schematic outline of the PI method for outbreak detection



Growth phase: Hidden Markov Model

- We used a two-state HMM to estimate the transition probability from pre-epidemic $(Z_t = 1)$ to growth $(Z_t = 2)$ state at each time point; with the following mathematical form:

$$\begin{pmatrix} 1-p_{12} & p_{12} \\ 0 & 1 \end{pmatrix} \text{ and } Y_t \sim NB(\mu_t, r_t), \text{ where}$$

$$\mu_{t|Z_{t=1}} = \mu_{t-1} \text{ and } \mu_{t|Z_{t=2}} = \mu_{t-1}e^{\beta_1},\ \beta_1 > 0$$

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- HMM was fitted in a Bayesian framework using Markov Chain Monte Carlo.
- An alert was raised when the posterior probability of transitioning from the pre-epidemic state to growth exceeded 50%.

Growth phase: HMM-PI approach

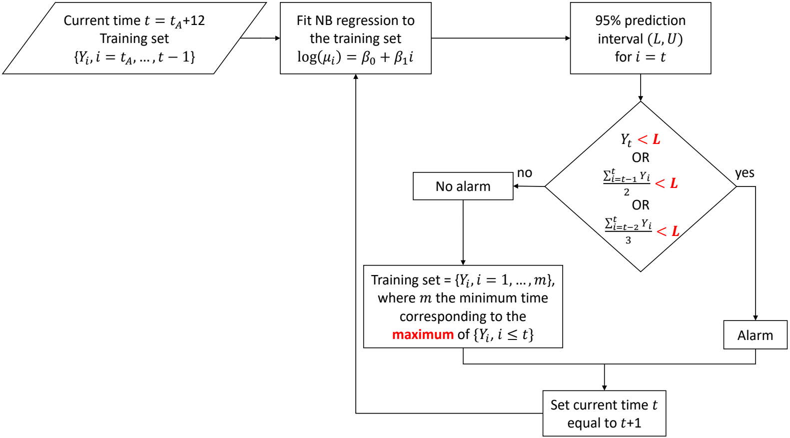
We proposed a new method, called HMM-PI, that combines HMM and PI by assigning weights to HMM's transition probabilities at each week based on the PI upper limit as follows:

$$\begin{pmatrix} w_t(1-p_{12}) & 1-w_t(1-p_{12}) \\ 0 & 1 \end{pmatrix}, \text{ where } w_t = \begin{cases} \frac{Y_t - U}{Y_t} & , Y_t > U \\ 1 & , Y_t \leq U \end{cases}$$

The weighting scheme was applied for a fixed time horizon (i.e, 12 weeks) after four consecutive alarm signals triggered by PI.

Decline and post-epidemic state: PI method

Schematic outline of the PI method for **decline** detection.



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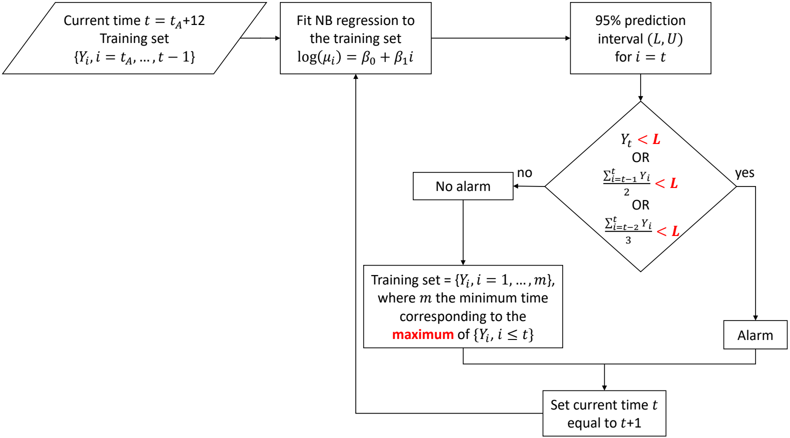

To identify the **post-epidemic** state, we used the PI method for outbreak detection.

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  - **from decline** $(Z_t = 3)$ **to post-epidemic** $(Z_t = 4)$ state

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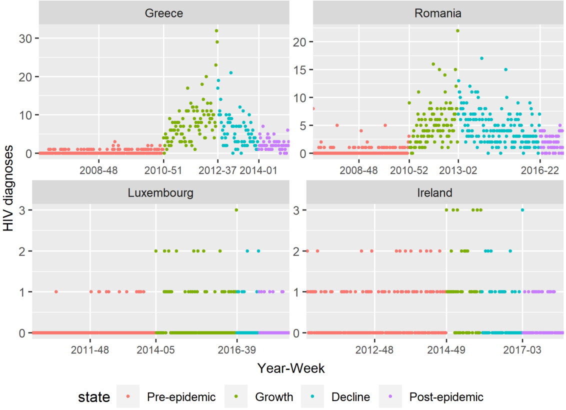
- HMM-PI combined HMM and PI integrating the appropriate transformations for the decline and post-epidemic state.

Data


Greece
Romania
Luxembourg
Ireland
HIV diagnoses
Year-Week
2008-48
2010-51
2012-37
2014-01
2008-48
2010-52
2013-02
2016-22
2011-48
2014-05
2016-39
2012-48
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2017-03
state
Pre-epidemic
Growth
Decline
Post-epidemic

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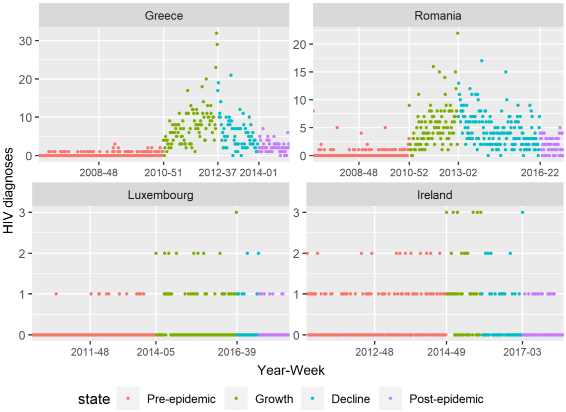

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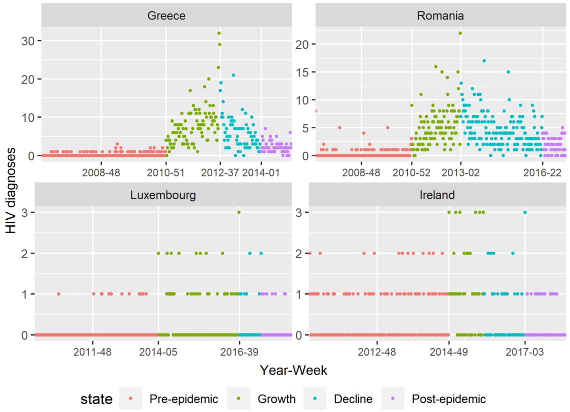

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- Data were provided by The European Surveillance System (TESSy) of European Centre for Disease Prevention and Control (ECDC).

Performance metrics

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  - timeliness: difference between the start of each state and the first alarm signal after its onset.

Results: Detection of small outbreaks

Key findings

- Extremely small outbreaks that returned to pre-epidemic levels
- Only control charts identified the growth and post-epidemic state.

Country	Method	Sensitivity	Specificity
Luxembourg	CUSUM	94%	<50%
	EWMA	55%	69%
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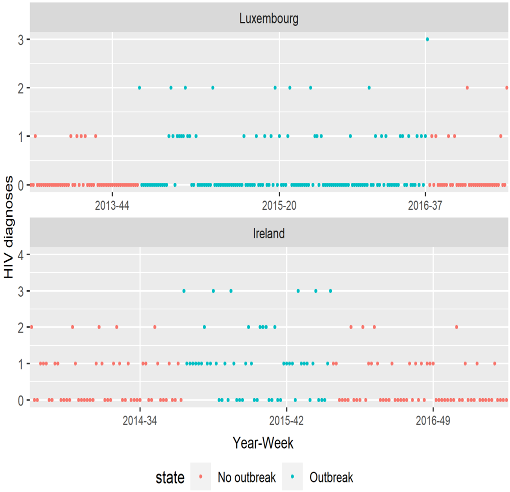

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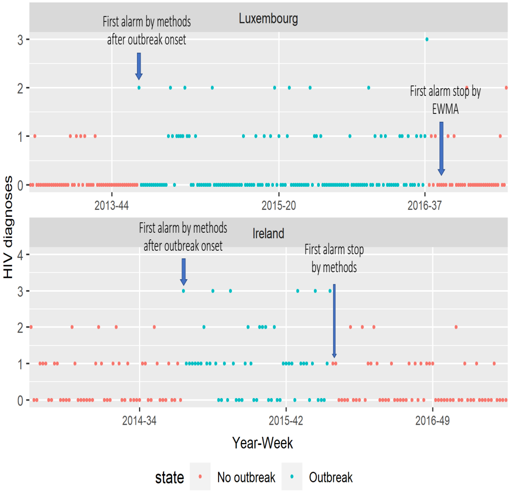

Results: Epidemic growth

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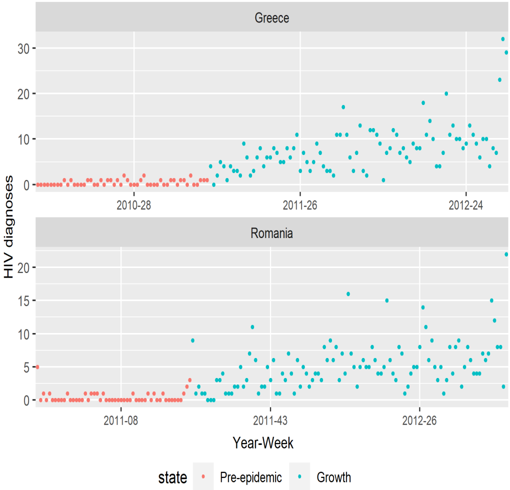
- Almost no delay in alarm
- PI performed at least similarly with control charts
- HMM-PI: excellent performance albeit with moderate specificity in Romania

Country	Method	Sensitivity	Specificity
Greece	CUSUM	100%	92%
	EWMA	100%	90%
	HMM	76%	100%
	PI	94%	100%
	HMM-PI	100%	100%
Romania	CUSUM	100%	85%
	EWMA	100%	90%
	HMM	59%	93%
	PI	87%	96%
	HMM-PI	100%	$\approx 50\%$



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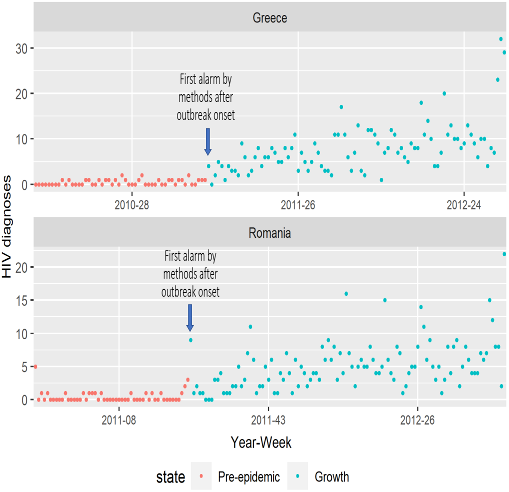

Results: Decline phase

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- Post-epidemic counts in Romania and Greece were stabilised at a level higher than the pre-epidemic ⇒ control charts failed.
- The remaining methods were applied for **decline** detection.

Country	Method	Sensitivity	Specificity	Timeliness (weeks)
Greece	HMM	85%	100%	10
	PI	<50%	100%	25
	HMM-PI	91%	100%	6
Romania	HMM	61%	98%	0
	PI	67%	94%	35
	HMM-PI	100%	77%	0

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Results: Post-epidemic state

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- PI performed better in both countries with:
  - 100% sensitivity,
  - no delay in triggering an alarm but
  - moderate specificity ($< 70\%$).

- When applied retrospectively (i.e., at the end of each state), the simple two-state HMM gave almost perfect performance in terms of sensitivity ($\approx 100\%$) and specificity ($\approx 100\%$).

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- We recommend HMM-PI and PI for monitoring large and abrupt outbreaks that do not return to pre-epidemic levels.
- Classic control charts are adequate for detecting the start and/or the end of very small epidemics.
- Although HMM did not reach a high real-time performance, it may provide useful insights when applied retrospectively.

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Thank You!